UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,614	04/15/2002	Yahia Gawad	3477.94	5111

20792 7590 12/13/2004

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,614	GAWAD, YAHIA	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 27-54* is/are pending in the application.

4a) Of the above claim(s) *28-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 41-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's cancellation of claim 26, and addition of claims 41-54 are acknowledged and have been entered.

2. Applicant's amendment of claims 1, 2, 5, 7, 8, 21, 23, and 27 is acknowledged and has been entered.

Rejections Withdrawn

3. Applicant's arguments, see page 13, filed September 22, 2004, with respect to rejection of claim 5 under 35 U.S.C. 112, second paragraph, have been fully considered and are persuasive. The rejection of claim 5 under 35 U.S.C. 112, second paragraph, has been withdrawn.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, while applicants disclose the selection of a calcium sensitive chemiluminescent material to obtain a short period of time between the flash emitted by the ultraviolet light source and the emission of light by the calcium-sensitive

luminescent material, as seen in page 15, applicants do not disclose the selection of calcium caging compound for this purpose.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-7, 10-12, 14-17, 19, 21-25, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pankratz et al [US 5,876,935] in view of Liotta et al [US 5,942,407].

With respect to claims 1, 2, 21, 23, 25, Pankratz et al teach a method comprising the steps of combining with a sample a binding reagent labeled with a luminescent molecule that is capable of binding to an analyte, contacting the sample with another binding reagent that can be biotinylated (column 5, lines 1-4), immobilized on a solid support such as superparamagnetic microspheres (column 7, example 2) by means of avidin or streptavidin (column 5 lines 1-4) so that a complex with the analyte bound to the labeled binding reagent is formed, activating the luminescent label in the solid support-free sample or in the complex bound to the solid support, and determining the presence of analyte in the sample by detecting the light emitted from the activated luminescent label (claim 1). Pankratz et al further teach that the label can be aequorin, and is activated by adding sufficient calcium ions (column 5, line 65-column 6, lines 4).

Pankratz fail to teach that the calcium ions are added by using ultraviolet light to effect the release of calcium from a caged calcium compound.

Liotta et al, however, do teach the use of a caged calcium compound immobilized in a support and using ultraviolet light to activate the compound (column 13, lines 25-35), in order to extend the duration of light emission resulting from analyte detection (column 13, lines 35-40).

Therefore it would have been obvious to include a caged calcium compound immobilized in a support and ultraviolet light to activate the compound in the method of Pankratz et al, in order to extend the duration of light emission resulting from analyte detection.

While neither Liotta et al nor Pankratz et al do not specifically teach that the calcium-sensitive luminescent material is selected to obtain a period of time between the flash emitted by the ultraviolet light source and the emission of light by the calcium-sensitive luminescent material, the calcium-sensitive luminescent material used by both Liotta et al and Pankratz et al is aequorin, and therefore such a period of time would be present in the method of Pankratz et al in view of Liotta et al.

8. With respect to claims 3, 14 Pankratz et al teach that the method is an immunoassay for detecting and quantifying an antigen (column 1, lines 13-22).

9. With respect to claims 4, 5, and 6, Liotta et al teach the use of calcium chelating agents such as EDTA or EGTA during one or more pretreatment steps (column 12, lines 53-56). Pankratz et al further teach that the solution is whole blood (claim 1).

10. With respect to claims 7, 17, Pankratz et al teach that the calcium-sensitive luminescent material is aequorin (claim 2).

11. With respect to claim 10, Liotta et al teach that the substrate can be comprised of nitrocellulose (column 11, lines 46-65).

12. With respect to claim 11, Liotta et al teach that the substrate comprises a transverse stripe with immobilized second binding partner and a calcium caging compound (column 12, lines 46-50, column 13, lines 15-45).

13. With respect to claim 12, Liotta et al teach that the calcium caging compound is loaded with an excess of calcium, in order to overcome any residual chelating agents from the pretreatment steps (column 13, lines 7-12).

14. With respect to claims 15, 16, Liotta et al teach that the binding assay can be an immunoassay or a nucleic acid hybridization assay (column 5, line 38 – column 6, line 50).

15. With respect to claim 19, Liotta et al teach that the luminescence is measured by a photomultiplier (column 13, lines 50-53).

16. With respect to claims 22, 24, Pankratz et al teach that all the component may be added at the same time, in which case the binding reactions would occur simultaneously (column 3, lines 40-45).

17. With respect to claim 26, Liotta et al teach that the timing of the caged calcium can extend the length of the light pulse, and provides a technique for performing multiple assays at once (fig 9A, 10, column 17, lines 17-30). Furthermore, Liotta et al teach that the light detection is performed by utilizing a shutter assembly which is opened for a predetermined amount of time, to detect the intensity of light emission (column 14, lines 29-45).

18. With respect to claim 27, Liotta et al teach the use of calcium chelating agents such as EDTA prior to the pulse of ultraviolet light. Although Liotta et al do not specifically state that the solution contains less than 20 nM of calcium, they teach the use of EDTA to remove any calcium in the solution (column 13, lines 10-14) such that any calcium remaining would be of a concentration less than 20 nM.

19. With respect to claims 41-48, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Therefore, it would have been obvious through normal optimization techniques known in the art to load the calcium-caging compound with up to 75% calcium, and for the free calcium concentration of the solution to be less than 20 nanomolars.

20. Claims 8, 9, 13, 18, 20, and 49-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pankratz et al [US 5,876,935] in view of Liotta et al [US 5,942,407], and further in view of Ellis-Davies et al [US 5,446,186].

With respect to claims 13, 49-54, Pankratz et al and Liotta et al teach a method of a binding assay as discussed above involving the use of aequorin and obelin (column 13, lines 15-25) and of caged calcium compounds. Neither Pankratz et al nor Liotta et al disclose specific caged calcium compounds.

21. Ellies-Davies et al, however, teach that compounds such as 1-(4,5 dimethoxy-2-nitrophenyl)-1, 2 diaminoethane-N, N, N', N'-tetraacetic acid (DM-nitrophen) and nitrophenyl-ethylenebis(oxyethylenennitrilo) tetraacetic acid (NP-EGTA) are well known in the art as calcium chelating compounds (column 1, lines 50-60, column 2, lines 6-20).

Ellies-Davies et al further teach that the compounds produce very high yields of liberated Ca^{2+} (column 1, lines 57-61, column 2, lines 10-15). Therefore it would have been obvious to use DM-nitrophen or NP-EGTA as the caged calcium compounds in the method of Pankratz et al and Liotta et al, as suggested by Ellis-Davies et al, in order to obtain high yields of liberated Ca^{2+}.

22. With respect to claims 8, 9, 18, and 20, Liotta et al teach the use of ultraviolet light at (column 13, lines 30-35) which can be in the form of a light pulse (column 17, lines 24-25), to activate the caged calcium compound. Ellis-Davies et al further specify the use of a laser at 347 nm (column 8, lines 25-32) liberates the Ca^{2+}. Liotta et al further teach that a photomultiplier is used to sense the luminescence (column 13, lines 49-53), which in the case of aequorin would be at about 470 nm (column 9, lines 57).

Response to Arguments

23. Applicant's arguments filed September 22, 2004 have been fully considered but they are not persuasive. Applicants argue that the prior art do not teach the selection of a calcium-sensitive chemiluminescent material and a calcium-caging compound such that there is a period with no light emission between the pulse of ultraviolet light effecting calcium release and the emission of luminescence by the luminescent material. While it is acknowledged that the prior art does not teach that there is a period with no light emission between the pulse of ultraviolet light effecting calcium release and the emission of luminescence by the luminescent material, it should be pointed out that on page 15 of the specification pointed out by applicants, applicants merely disclose that the calcium-sensitive luminescent material itself is selected to obtain such a period of time. Furthermore, applicants disclose that aequorin is one such material, which is the calcium-

sensitive chemiluminescent material taught by the prior art. Therefore, the claim would still read on the prior art.

24. Applicants may wish to further clarify if there are additional limitations besides the selection of the calcium-sensitive luminescent material that would be responsible for the period with no light emission between the pulse of ultraviolet light effecting calcium release and the emission of luminescence by the luminescent material.

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
12/10/01